

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/012459

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 G01N33/574 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KOHLMANN A ET AL: "MOLECULAR CHARACTERIZATION OF ACUTE LEUKEMIAS BY USE OF MICROARRAY TECHNOLOGY" GENES, CHROMOSOMES & CANCER, XX, XX, vol. 37, no. 4, August 2003 (2003-08), pages 396-405, XP008025253 the whole document in particular table 3 ----- -/-	1-27

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the International filing date but later than the priority date claimed

- \*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the Invention
- \*X\* document of particular relevance; the claimed Invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed Invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the International search

2 March 2005

Date of mailing of the International search report

28 06, 2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Thumb, W

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/012459

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TSUTSUMI SHUICHI ET AL: "Two distinct gene expression signatures in pediatric acute lymphoblastic leukemia with MLL rearrangements." CANCER RESEARCH, vol. 63, no. 16, 15 August 2003 (2003-08-15), pages 4882-4887, XP002272402 ISSN: 0008-5472 (ISSN print) the whole document	1-27
Y	YEOH E-J ET AL: "Classification, subtype discovery, and prediction of outcome in pediatric acute lymphoblastic leukemia by gene expression profiling" CANCER CELL, XX, US, vol. 1, no. 2, March 2002 (2002-03), pages 133-143, XP002253604 ISSN: 1535-6108 the whole document	1-27
Y	WO 03/039443 A (DEUTSCHES KREBSFORSCH ; HAFLERLACH TORSTEN (DE); EILS ROLAND (DE); K) 15 May 2003 (2003-05-15) the whole document, in particular pages 71 and 72	1-27
Y	WO 03/083140 A (WONG LIMSOON ; YEOH ENG-JUH (SG); DOWNING JAMES R (US); WILKINS DAW) 9 October 2003 (2003-10-09) the whole document	1-27
Y	CHEN JIANN-SHIUH ET AL: "Identification of novel markers for monitoring minimal residual disease in acute lymphoblastic leukemia" BLOOD, vol. 97, no. 7, 1 April 2001 (2001-04-01), pages 2115-2120, XP002272403 ISSN: 0006-4971 the whole document	1-27
Y	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), KOHLMANN ALEXANDER ET AL: "Functionally Annotated Gene Expression Profiles of t(9;22) Positive CML and ALL." XP002272404 Database accession no. PREV200300335812 abstract	1-27

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/012459

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	& BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 1212, 44th Annual Meeting of the American Society of Hematology; Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971 ----- EP 1 043 676 A (WHITEHEAD BIOMEDICAL INST) 11 October 2000 (2000-10-11) the whole document -----	1-27
Y	GOLUB T R ET AL: "Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 286, no. 5439, 15 October 1999 (1999-10-15), pages 531-537, XP002207658 ISSN: 0036-8075 cited in the application the whole document -----	1-27
Y	DUGAS M ET AL: "A comprehensive leukemia database: integration of cytogenetics, molecular genetics and microarray data with clinical information, cytomorphology and immunophenotyping" LEUKEMIA, MACMILLAN PRESS LTD, US, vol. 15, no. 12, December 2001 (2001-12), pages 1805-1810, XP002263731 ISSN: 0887-6924 the whole document -----	1-27
Y	DUGAS MARTIN ET AL: "Impact of integrating clinical and genetic information." IN SILICO BIOLOGY, vol. 2, no. 3, 2002, pages 383-391, XP001179418 ISSN: 1386-6338 (ISSN print) the whole document -----	1-27
		-/-

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/012459

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ALIZADEH A ET AL: "THE LYMPHOCHIP: A SPECIALIZED CDNA MICROARRAY FOR THE GENOMIC-SCALE ANALYSIS OF GENE EXPRESSION IN NORMAL AND MALIGNANT LYMPHOCYTES"</p> <p>COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY, BIOLOGICAL LABORATORY, COLD SPRING HARBOR, NY, US, vol. 64, no. 1, 1999, pages 71-78, XP001099007 ISSN: 0091-7451 the whole document</p> <p>-----</p>	1-27
A	<p>DATABASE BIOSIS 'Online!' BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), KOHLMANN ALEXANDER ET AL: "A Simplified and Partially Automated Target Preparation Method for Gene Expression Profiling." XP002269495 Database accession no. PREV200300367771 abstract &amp; BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 4287, 44th Annual Meeting of the American Society of Hematology; Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971</p> <p>-----</p>	1-27
A	<p>DEUTSCH J M: "Evolutionary algorithms for finding optimal gene sets in microarray prediction." BIOINFORMATICS (OXFORD), vol. 19, no. 1, January 2003 (2003-01), pages 45-52, XP002272405 ISSN: 1367-4803 the whole document</p> <p>-----</p>	1-27

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2004/012459

### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

#### Article 52 (2)(d) EPC – Presentation of information

The claims were only searched with regards to the underlying method of generating a reference data base for distinguishing immunologically defined

2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-27 (partially)

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Article 52 (2)(d) EPC - Presentation of information

The claims were only searched with regards to the underlying method of generating a reference data base for distinguishing immunologically defined ALL subtypes.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-27 (partially)

A method for distinguishing mature B-ALL from all other subtypes of immunologically defined ALL subtypes, the method comprising determining the expression level of the marker CD99. Use of said marker for the manufacture of a diagnostic. A diagnostic kit containing said marker and an apparatus comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression level of CD99.

---

2. claims: 1-27 (all partially)

Inventions 2-1050

Methods for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL and/or T-ALL and methods for distinguishing specific subtypes against all other subtypes and against each other, the method comprising determining individually the expression level of the markers listed in tables 1.1, positions 2-50, tables 1.2-1.6 and in table 2. Use of said markers for the manufacture of diagnostics. Diagnostic kits containing said markers and apparatus comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression levels of said markers.

---

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/012459

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 03039443	A	15-05-2003	EP	1308522 A1		07-05-2003
			WO	03039443 A2		15-05-2003
			EP	1470247 A2		27-10-2004
WO 03083140	A	09-10-2003	AU	2003231969 A1		13-10-2003
			WO	03083140 A2		09-10-2003
			US	2004018513 A1		29-01-2004
EP 1043676	A	11-10-2000	CA	2304876 A1		09-10-2000
			EP	1043676 A2		11-10-2000
			JP	2001017171 A		23-01-2001
			US	2003017481 A1		23-01-2003
			US	6647341 B1		11-11-2003
			US	2003073083 A1		17-04-2003